Effect of L-arginine on cardiac function and fibrosis in *mdx* mice

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The primary cause of Duchenne Muscular Dystrophy, a condition that affects 1 in 3500 live male births, is a deficiency of the protein dystrophin. This deficiency leads to downregulation of the neuronal nitric oxide synthase (nNOS) and lowered production of nitric oxide. This study investigated the effects of L-arginine, the substrate of nNOS, on cardiac function and fibrosis in *mdx* mice, a widely used animal model for Duchenne Muscular Dystrophy. Six month old *mdx* mice received 5 mg/g body weight L-arginine by daily oral gavage for six months while control *mdx* and C57BL10ScSn mice received water by oral gavage. At the completion of treatment, mice were anaesthetised with sodium pentobarbitone (70 mg/kg, i.p.) prior to euthanasia by excision of the heart. Cardiac function was assessed with the Langendorff technique at a perfusion pressure of 80 mmHg. *Mdx* mice had an impaired left ventricular developed pressure relative to C57BL10ScSn control mice, but this difference was not evident in L-arginine treated *mdx* mice. The L-arginine treated *mdx* mice also showed an increased coronary flow and reduced diastolic stiffness relative to untreated *mdx* mice ($P<0.05$). This reduction in stiffness was associated with a significant reduction in cardiac collagen measured as the percent of left ventricular area stained with the collagen specific dye picrosirius red ($P<0.05$). These results indicate that chronic treatment with L-arginine produces the beneficial effects of improving function and reducing fibrosis in the dystrophin-deficient heart.